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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/396,985 09/15/99 BEUTLER

B TSD:602

EXAMINER

HM22/0814

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BASILIN

ART UNIT

PAPER NUMBER

1646

DATE MAILED:

08/14/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/396,985

Applicant(s)

BEUTLER ET AL

Examiner

Nirmal. S. Basi

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on May 25, 2001
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 38-40 and 52-75 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 38-40 and 52-75 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- *See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892)
- 16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
- 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 19) ☐ Notice of Informal Patent Application (PTO-152)
- 20) ☐ Other:

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DETAILED ACTION

1. Amendment filed 2/7/01 and 5/25/01 have been entered.

Claim Rejection, 35 U.S.C. 112, second paragraph

2. Claims 38-40, 52-75 and 100 are rejected under 35 U.S.C. 112, second paragraph, as being
5 indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 38, 40, 52 and 62 are indefinite because the name TLR-4 has not been defined in the claims and specification so as to allow the metes and bounds of the claims to be determined. Applicant argues TLR-4 has been defined to meet the requirements of 35 USC 112, second
10 paragraph. Applicants arguments have been fully considered but not found persuasive. The name TLR-4 polypeptide is not an art accepted term and does not provide any structural or functional properties of the polypeptide. Further the name TLR-4 is subject to change, and may lead to ambiguity. Applicants states on page 6, of paper number 11, filed 2/7/01, that the name has already been changed once from Toll-4 to TLR-4. Similarly other proteins may have different names, but
15 encompass the same protein. Therefore without a clear disclosure of the structure and function of the TLR-4 protein the metes and bounds of the claim cannot be determined.

Claim 38 is indefinite because it is not clear what is a "lipopolysaccharide mediated response" and what parameters are screened to determine the response. The "lipopolysaccharide mediated response" and the parameters screened to determine the response are not defined so as to allow the
20 metes and bounds of the claim to be determined. Further in step it is not clear how the standard

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activity profile is determined? What is the “standard activity profile”? What parameters are measured to assign a value to the “standard activity profile”? An acceptable method claim must contain three sections: 1) a preamble, 2) method steps that clearly define what is to be done in each step, and 3) a conclusion that what was stated in the preamble was achieved (the method does not contain an assay step which states how and when the goal of the claim is achieved).

Claim 52 is indefinite because it is not clear what is “function” of the modulator effected and what are the boundaries of the lipopolysaccharide pathway so as to allow the meets and bounds of the claim to be determined. Where does the “lipopolysaccharide pathway” begin and end?

Claim 62 is indefinite because it is not clear what are the “conditions that normally allow for TLR-4 transcription”, so as to allow the metes and bounds of the claim to be determined.

is “function” of the modulator effected and what are the boundaries of the lipopolysaccharide pathway so as to allow the meets and bounds of the claim to be determined. Where does the “lipopolysaccharide pathway” begin and end?

Claims 40 is indefinite because it is not clear what is the reporter gene, what said gene reports and what is the promotor from a TLR-4 gene so as to allow the metes and bounds of the claim to be determined. Applicant argues the definition of the reporter gene but does not disclose where in the specification it is defined. Further, the claim does not disclose what the “reporter gene “ reports.

Claims 40 is indefinite because it is not clear what is a “standard activity profile”, what it measures and how it is assayed so as to allow the metes and bounds of the claim to be determined.

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Claim 52 is indefinite because it is not clear what “function” of TLR-4 is affected.

Claims 52, 55, 56 and 62-64 are indefinite because it is not clear what is a TLR-4. “TLR-4” is indefinite for reasons given above.

Claim 69 is indefinite because it is not clear what is a, “small molecule inhibitor”, so as to allow the metes and bounds of the claim to be determined. What small molecule is being inhibited? When is a compound considered small so as to allow the meets and bounds of the claim to be determined.

Claim 71 is indefinite because “stimulator of an immune response” does not provide any structural limitations to the modulator and to what parameter is stimulated in the immune response, so as to allow the metes and bounds of the claim to be determined.

Claims 39, 53-54, 57-61, 65, 66, , 68, 70, 72-75 are indefinite for depending on a base claim or intermediate claim and fail to resolve the issues raised above.

Applicants arguments have been fully considered regarding the rejections of the above claims under 35 U.S.C. 112, second paragraph, but not found persuasive for the reasons given above.

Claim Rejection, 35 U.S.C. 112

3. Claims 38-40, 52-75 and 100 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a screening method for compounds which modulate a LPS mediated response by inducing the synthesis or altering expression of TLR-4 of SEQ ID NOs: 2, 4, 6, 98 and 99, does not reasonably provide enablement for other methods of screening for

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compounds which may affect any other LPS-mediated responses or methods for identification of compounds which may predictably have other activities by any way other means than the altered expression of TLR-4 (SEQ ID Nos:2, 4, 6, 98 and 99). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Applicants arguments have been fully considered but not found persuasive for the reasons given below.

The claims are directed to screening for modulators of a LPS mediated response. The specification discloses that TLR-4 mRNA is induced by LPS (Fig 9) and TLR4 is the limiting factor in LPS signal transduction in LPS responsive macrophages, the quantity of TLR4 expressed is an important limiting factor in the intensity of the signal that is evoked (page 128). The specification discloses the screening of modulators of LPS mediated response where the compounds screened can modulate the expression of TLR-4 of SEQ ID NOs:2, 4, 6, 98 and 99. The scope of the claims which encompasses other methods of screening for modulators of LPS, using proteins other than those disclosed in SEQ ID NOs:2, 4, 6, 98 and 99, where the compounds may have activity by other means than the altered expression of TLR-4 expression of SEQ ID NOs:2, 4, 6, 98 and 99 is not enabled by the disclosure.. For the person of ordinary skill in the art to screen for modulators of a LPS mediated response by any other means than those disclosed as “enabling” above, the artisan must first isolate other proteins capable of direct or indirect interaction with LPS and its modulators, and develop screening assays to determine if certain compounds can be modulators of the LPS mediated response. Therefore, the lack of guidance provided in the specification as to what

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other assays may be used to screen for modulators of LPS, unpredictability and undue experimentation in isolating other TLR-4 polypeptides would prevent the skilled artisan from practicing the invention in its full scope.

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No claim is allowed

Advisory Information

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal Basi whose telephone number is (703) 308-9435. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 308-0294.

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Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nirmal S. Basi
Art Unit 1646
August 13, 2001

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Michael D. Pak
MICHAEL PAK
PRIMARY EXAMINER